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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,955	05/10/2006	Robert K. Evans	21575P	8652

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MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
01/19/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,955	EVANS ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 21-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 21-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/13/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 13, 2009 has been entered. Claims 1-10 and 21-32 are pending and under examination.

Claims Summary

2. The claims are directed to a live adenovirus formulation comprising 0.25% to 0.6% (w/v), or 0.4% to 0.6% (w/v) chlorobutanol (CB), and a buffer within a pH range of about 6.0 to about 9.0. Other components include various inhibitors of free radical oxidation, cryoprotectants, salts, divalent cations and non-ionic detergents. Also claimed is a vaccine vial comprising the formulation, and a method of preserving a live adenovirus formulation.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 9, 10, 21, 22 and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gao *et al.* (WO 01/40455 A2, "Gao"). The claims are summarized above. Gao discloses live, recombinant adenovirus vectors for pharmaceutical use comprising a preservative, such as chlorobutanol (see page 19, first paragraph), and a buffer, such as PBS (page 18, lines 21-26). The adenovirus concentration taught by Gao is in the range of 10^{10} to 10^{18} for an adult human having a weight of about 80 Kg (see page 19, fourth paragraph).

Gao fails to teach the specific range of CB concentration. However, it would have been well within the ability of the ordinary artisan to determine which concentration of CB would have been appropriate for preserving the live adenovirus vectors. Given Gao's suggestion to use CB, the ordinary artisan would have then performed routine tests to determine the concentration of CB that can preserve the live viruses without compromising the integrity of the viruses.

Gao suggests the use of a buffer, but does not specifically teach a composition buffer within a pH range of about 6.0 to about 9.0. However, it would have been well within the ability of the ordinary artisan to determine a suitable buffer and pH for the adenovirus/preservative composition. Given Gao's suggestion to use a buffer, which is also a standard practice in the art for stabilization purposes, the ordinary artisan would have then determined the appropriate pH for the composition without compromising the integrity of the preserved viruses.

Gao does not specifically teach that the formulation of live adenovirus contains CB in the amount of a lowest effective concentration of CB up to the solubility limit of CB for the formulation. However, Gao teaches that CB is used as a preservative in a live, recombinant adenovirus composition for administration. It would have been obvious to one of ordinary skill

in the art and well within the ability of that individual to use an amount of CB that is effective for the purpose of preservation without exceeding the solubility limit for the formulation.

Gao does not specifically teach the use of a multi-dose or single dose vial, however it would have been obvious to use a vial to store the contents of the formulation in order to contain and protect the formulation for delivery, storage and subsequent use. Gao discloses that the formulation of live, recombinant adenovirus can be administered using any suitable route, such as intravenous, intramuscular, etc. (see page 19, second paragraph). If one were to administer Gao's composition using a needle, then the formulation would necessarily come from a vial of some sort. As for the multi-dose or single dose vial, it would have been obvious and well within the ability of the ordinary artisan to package the contents of the vials according to the desired use. Gao teaches that the dose may be repeated as desired (see page 19, fourth paragraph).

Therefore, the claimed embodiments would have been obvious at the time the invention was made.

Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant argues that Gao does not teach any buffer having a pH within a range of about 6.0 to about 9.0. Applicant asserts that the art teaches that CB is not stable in buffered solutions greater than pH 6, see Taub *et al.* (*J. Amer. Pharm. Assoc.*, 1943) and Patwa *et al.*, (*J. Amer. Pharm. Assoc.*, 1943). Applicant also points to Akers (*Pharm. Technol.*, 1984) which discloses that CB is not effective as a preservative at a pH of 5 or greater.
  - In response to Applicant's argument, the Office notes that the claims encompass a composition comprising a buffer that has a pH range of about 6.0 to about 9.0. The

term "about 6.0" is not a clear cut-off point. The interpretation of the term "about 6.0" is broad and subject to individual interpretation.

- With regard to the Taub *et al.* and Patwa *et al.* references, one of ordinary skill in the art would conclude that the stability of CB in buffered solutions is between 3-6. Note that the claims do not exclude a pH below 6.0, since "about 6.0" (recited in claim 1) is not a clear cut-off point and does not exclude values below 6.0. (With regard to the Akers reference, it is not clear if the CB solution was buffered.)

- Applicant argues that the specification provides unexpected results relative to the prior art. For example, Table 7 shows that CB buffered at pH 7.4 (A195 buffer) provided effective antimicrobial activity and passed USP criteria and EP criteria B. Applicant argues that these results, compared with the prior art's teachings about CB buffered solutions being effective between 3-6, show that the claimed invention provides unexpected results.

  - In response to Applicant's argument, the unexpected results with regard to buffer A195 (10 mM Tris and 10 mM histidine at pH 7.4) plus 0.4% or 0.5% CB appear to be particular to these specific conditions since other formulations do not appear to have had the unexpected result. The claims are not limited to the embodiment that yielded the unexpected results, nor is the pH recited in the claims limited to a range that clearly excludes pH 3-6. Therefore, the rejection is maintained for reasons of record and in view of the above discussion.

4. Claims 3-8 and 23-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gao *et al*. (WO 01/40455 A2, "Gao") as applied to claims 1 and 21 above, and further in view of Evans *et al*. (WO 01/66137 A1, "Evans"), for reasons of record. Applicant's arguments have been addressed above.

Conclusion

5. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B Chen/
Primary Examiner, Art Unit 1648